PDGF signaling is required for epicardial function and blood vessel formation in regenerating zebrafish hearts.

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Public Summary:

Scientific Abstract:
A zebrafish heart can fully regenerate after amputation of up to 20% of its ventricle. During this process, newly formed coronary blood vessels revascularize the regenerating tissue. The formation of coronary blood vessels during zebrafish heart regeneration likely recapitulates embryonic coronary vessel development, which involves the activation and proliferation of the epicardium, followed by an epithelial-to-mesenchymal transition. The molecular and cellular mechanisms underlying these processes are not well understood. We examined the role of PDGF signaling in explant-derived primary cultured epicardial cells in vitro and in regenerating zebrafish hearts in vivo. We observed that mural and mesenchymal cell markers, including pdgfrbeta, are up-regulated in the regenerating hearts. Using a primary culture of epicardial cells derived from heart explants, we found that PDGF signaling is essential for epicardial cell proliferation. PDGF also induces stress fibers and loss of cell-cell contacts of epicardial cells in explant culture. This effect is mediated by Rho-associated protein kinase. Inhibition of PDGF signaling in vivo impairs epicardial cell proliferation, expression of mesenchymal and mural cell markers, and coronary blood vessel formation. Our data suggest that PDGF signaling plays important roles in epicardial function and coronary vessel formation during heart regeneration in zebrafish.

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